DOCKET NO.: ISIS-4789 **Application No.:** 09/970,971 **Office Action Dated:** October 20, 2004

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

REMARKS

Claims 1-13, 18 and 21-32 are pending in this patent application.

As a preliminary matter, Applicants thank Examiner Owens for having a telephonic interview with their attorney, Jeffrey H. Rosedale, on November 23, 2004. Examiner Owens confirmed for Mr. Rosedale that the rejections under 35 U.S.C. §§ 102(b) and 103(a) over U.S. Patent No. 5,670,633 to Cook et al. ("the 633 patent") appear to be improper. Accordingly, Applicants address the remaining alleged double patenting rejection below.

I. Alleged Obviousness-Type Double Patenting

Claims 1-13, 18, and 21-32 continue to stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-25 of U.S. Patent No. 6,369,209 ("the 209 patent") in view of Damha, et al., Bioconjugate Chemistry, 1999, 10, 299 ("the Damha reference"). Applicants respectfully traverse this rejection because the Office Action fails to establish a prima facie case of obviousness. The Federal Circuit has held that an examiner's showing with respect to obviousness-type double patenting rejection must conform to that required to establish a prima facie case of obviousness. In re Longi, 225 USPQ 645, 651 (Fed. Cir. 1985). "Since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. 103 rejection," the MPEP mandates that "the factual inquiries set forth in Graham v. John Deere, Co. 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 [be] employed when making an obviousness-type double patent analysis." MPEP § 804.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on

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applicant's disclosure. MPEP § 2143, *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The Office Action, however, does not provide any analysis of the *Graham* factors or otherwise make out a *prima facie* case of obviousness of the **claimed invention**. Rather, the instant Office Action (and the Office Action mailed March 12, 2004) improperly focus on **limitations that do not appear in the claims.** For example, the instant Office Action asserts that one of skill in the art would have been motivated to substitute an arabinose as the pentosyl moiety in a duplex oligonucleotide:

"Claims 1-25 of '209 are drawn to analogous oligonucleotides; however, the B-form of the first portion contains at least 2 **arabino**nucleotides.

Damha teaches that the substitution of **arabinose** as the pentosyl moiety confers more stability to serum and cellular nucleases than DNA.

It would have been prima facie obvious to substitute an arabinose as the pentosyl moiety in a duplex oligonucleotide.

One of skill in the art would have been motivated to substitute an **arabinose** as the pentosyl moiety in a duplex oligonucleotide to provide even greater resistance to nuclease attack."

(Office Action mailed March 12, 2004, at page 3, emphasis supplied). However, neither arabinose nor arabinonucleotides are required by the instant claims. In addition, the Office Action fails to establish a *prima facie* case of obviousness for at least three reasons:

- (1) the Office Action does not identify some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the 209 patent claims with the Damha reference to arrive at the oligonucleotides that include the "at least two ... ribonucleotides" limitation of claim 1¹;
- (2) the Office Action does not explain why those of ordinary skill in the art would have had a reasonable expectation of success of arriving at the

¹ Instead, as discussed below, the Office Action discusses the motivation for substituting into the 209 patent claims a limitation (an arabinose sugar) that does not appear in instant claim 1.

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oligonucleotides that include the "at least two ... ribonucleotides" limitation of claim 1; and

(3) the Office Action does not explain how the combination of the 209 patent claims and the Damha reference teaches or suggests all of the limitations of the instant claims, for example the "at least two ... ribonucleotides" limitation of claim 1.

Absent such explanations (together with evidence supporting them), the rejections for alleged obviousness-type double patenting lack adequate support.

Indeed, neither the 209 patent claims nor the Damha reference so much as suggests the instantly claimed oligonucleotides. Arabinonucleotides are not ribonucleotides, and it appears to be for this reason that the Office Action acknowledges a failure of disclosure in the 209 patent claims with respect to Applicants' claimed subject matter. Specifically, the 209 patent claims do not mention the "at least two ... ribonucleotides" limitation of instant claim 1, and the Damha reference does not remedy this deficiency. Indeed, the Damha reference has not been relied upon for any disclosure relating to ribonucleotides. Rather, the Office Action appears to assert that the Damha reference teaches the advantages of arabinonucleotides, and thus would have motivated those of ordinary skill to include more than two arabinonucleotides in the oligonucleotides claimed in the 209 patent. Significantly, however, disclosure relating to Applicants' "at least two ... ribonucleotides" limitation would still have been lacking.

Since neither the 209 patent claims nor the Damha reference teach or suggest the claimed oligonucleotides, Applicants request that the rejection for alleged obviousness-type double patenting be reconsidered and withdrawn.

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In view of the foregoing, Applicants submit that the claims presently before the Examiner are in condition for allowance. An early Office Action to that effect is, therefore, earnestly solicited.

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Jeffrey H. Rosedale Registration No. 46,018

Woodcock Washburn LLP One Liberty Place - 46th Floor Philadelphia PA 19103

Telephone: (215) 568-3100 Facsimile: (215) 568-3439